



**DEPARTMENT OF JUSTICE**

**Drug Enforcement Administration**

**21 CFR Part 1308**

**[Docket No. DEA-434]**

**Schedules of Controlled Substances: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl into Schedule I**

**AGENCY:** Drug Enforcement Administration, Department of Justice

**ACTION:** Notice of intent.

**SUMMARY:** The Administrator of the Drug Enforcement Administration is issuing this notice of intent to temporarily schedule the synthetic opioids, *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutyramide (butyryl fentanyl) and *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide (beta-hydroxythiofentanyl), into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of these synthetic opioids into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, and exportation of, and research and conduct with, instructional activities of these synthetic opioids.

**DATES:** [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

**FOR FURTHER INFORMATION CONTACT:** Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

**SUPPLEMENTARY INFORMATION:** Any final order will be published in the *Federal Register* and may not be effective prior to [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

### **Legal Authority**

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801–971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, each controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause.

21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, 21 U.S.C. 811, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

## **Background**

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.<sup>1</sup> The

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<sup>1</sup> As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

Administrator transmitted notice of his intent to place butyryl fentanyl and beta-hydroxythiofentanyl in schedule I on a temporary basis to the Assistant Secretary by letter dated December 21, 2015 (received by the HHS on December 23, 2015). The Assistant Secretary responded to this notice by letter dated January 13, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for butryl fentanyl or beta-hydroxythiofentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of butryl fentanyl or beta-hydroxythiofentanyl into schedule I of the CSA. Neither butryl fentanyl nor beta-hydroxythiofentanyl are currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for butryl fentanyl or beta-hydroxythiofentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of butryl fentanyl and beta-hydroxythiofentanyl in schedule I on a temporary basis are necessary to avoid an imminent hazard to public safety.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(c): the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed in schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that

have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1).

#### **Butyryl Fentanyl and Beta-Hydroxythiofentanyl**

Available data and information for butyryl fentanyl and beta-hydroxythiofentanyl, summarized below, indicate that these synthetic opioid substances have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's three-factor analysis is available in its entirety under of the public docket of this action as a supporting document at [www.regulations.gov](http://www.regulations.gov) under Docket Number DEA-434.

#### **Factor 4. History and Current Pattern of Abuse**

Clandestinely produced substances structurally related to the schedule II opioid analgesic fentanyl were trafficked and abused on the West Coast in the late 1970s and 1980s. These clandestinely produced fentanyl-like substances were commonly known as designer drugs, and recently there has been a reemergence in the trafficking and abuse of designer drug substances, including fentanyl-like substances. Alpha-methylfentanyl, the first fentanyl analogue identified in California, was placed into schedule I of the CSA in September 1981. 46 FR 46799. Following the control of alpha-methylfentanyl, the DEA identified several other fentanyl analogues (3-methylthiofentanyl, acetyl-alpha-methylfentanyl, beta-hydroxy-3-methylfentanyl, alpha-methylthiofentanyl, thiofentanyl, beta-hydroxyfentanyl, para-fluorofentanyl, and 3-methylfentanyl) in submissions to forensic laboratories. These substances were temporarily controlled under schedule I of the CSA after finding that they posed an imminent hazard to public safety and were

subsequently permanently placed in schedule I of the CSA. On July 17, 2015, acetyl fentanyl was temporarily controlled under schedule I of the CSA after a finding by the Administrator that it posed an imminent hazard to public safety. 80 FR 42381.

Prior to October 1, 2014, the System to Retrieve Information from Drug Evidence (STRIDE) collected the results of drug evidence analyzed at DEA laboratories and reflected evidence submitted by the DEA, other federal law enforcement agencies, and some local law enforcement agencies. STRIDE data were queried through September 30, 2014, by date submitted to federal forensic laboratories. Since October 1, 2014, STARLiMS (a web-based, commercial laboratory information management system) has replaced STRIDE as the DEA laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are repositied in STARLiMS. Data from STRIDE and STARLiMS were queried on December 21, 2015. The National Forensic Laboratory Information System (NFLIS) is a program of the DEA that collects drug identification results from drug cases analyzed by other federal, state, and local forensic laboratories. NFLIS reports from other federal, state, and local forensic laboratories were queried on December 22, 2015.<sup>2</sup>

The first laboratory submission of butyryl fentanyl was recorded in Kansas in March 2014 according to NFLIS. STRIDE, STARLiMS and NFLIS registered seven reports containing butyryl fentanyl in 2014 in Illinois, Kansas, Minnesota, and Pennsylvania; 81 reports of butyryl fentanyl were recorded in 2015 in California, Connecticut, Florida, Indiana, North Dakota, New York, Ohio, Oregon, Tennessee, Virginia, and Wisconsin. A total of three reports of beta-hydroxythiofentanyl were recorded by STARLiMS, all of

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<sup>2</sup> Data are still being reported for September–November 2015, due to normal lag time for laboratories to report to NFLIS.

which were reported in 2015 from Florida. To date, beta-hydroxythiofentanyl has not been reported in NFLIS; however, this substance was identified in June 2015 by a forensic laboratory in Oregon.

Evidence also suggests that the pattern of abuse of fentanyl analogues, including butyryl fentanyl and beta-hydroxythiofentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of butyryl fentanyl have been encountered in tablet and powder form. Butyryl fentanyl was identified on bottle caps and spoons and residue was detected within glassine bags, on digital scales, and on sifters which demonstrates the abuse of this substance as a replacement for heroin or other opioids, either knowingly or unknowingly. Butyryl fentanyl has been encountered as a single substance as well as in combination with other illicit substances, such as acetyl fentanyl, heroin, cocaine, or methamphetamine. Like butyryl fentanyl, beta-hydroxythiofentanyl has been encountered in both tablet and powder form. Both butyryl fentanyl and beta-hydroxythiofentanyl have caused fatal overdoses, in which intravenous routes of administration are documented.

#### **Factor 5. Scope, Duration and Significance of Abuse**

The DEA is currently aware of at least 40 confirmed fatalities associated with butyryl fentanyl and 7 confirmed fatalities associated with beta-hydroxythiofentanyl. The information on these deaths occurring in 2015 was collected from toxicology and medical examiner reports and was reported from four states—Florida (7, beta-hydroxythiofentanyl), Maryland (1, butyryl fentanyl), New York (38, butyryl fentanyl), and Oregon (1, butyryl fentanyl). STRIDE, STARLiMS, and NFLIS have a total of 88 drug reports in which butyryl fentanyl was identified in drug exhibits submitted in 2014

and 2015 from California, Connecticut, Florida, Illinois, Indiana, Kansas, Minnesota, North Dakota, New York, Ohio, Oregon, Pennsylvania, Tennessee, Virginia, and Wisconsin. STARLiMS has a total of three drug reports in which beta-hydroxythiofentanyl was identified in drug exhibits submitted in 2015 from Florida. It is likely that the prevalence of butyryl fentanyl and beta-hydroxythiofentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays cannot differentiate these substances from fentanyl.

The population likely to abuse butyryl fentanyl and beta-hydroxythiofentanyl overlaps with the populations abusing prescription opioid analgesics and heroin. This is evidenced by the routes of administration and drug use history documented in butyryl fentanyl and beta-hydroxythiofentanyl fatal overdose cases. Because abusers of these fentanyl analogues are likely to obtain these substances through illicit sources, the identity, purity, and quantity is uncertain and inconsistent, thus posing significant adverse health risks to abusers of butyryl fentanyl and beta-hydroxythiofentanyl. Individuals who initiate (i.e. use an illicit drug for the first time) butyryl fentanyl or beta-hydroxythiofentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

#### **Factor 6. What, if Any, Risk There Is to the Public Health**

Butyryl fentanyl and beta-hydroxythiofentanyl exhibit pharmacological profiles similar to that of fentanyl and other mu-opioid receptor agonists. Due to limited scientific data, their potency and toxicity are not known; however, the toxic effects of both butyryl fentanyl and beta-hydroxythiofentanyl in humans are demonstrated by



overdose fatalities involving these substances. Abusers of these fentanyl analogues may not know the origin, identity, or purity of these substances, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on the documented case reports of overdose fatalities, the abuse of butyryl fentanyl and beta-hydroxythiofentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

Butyryl fentanyl and beta-hydroxythiofentanyl have been associated with numerous fatalities. At least 40 confirmed overdose deaths involving butyryl fentanyl abuse have been reported in Maryland (1), New York (38), and Oregon (1) in 2015. At least seven confirmed overdose fatalities involving beta-hydroxythiofentanyl have been reported in Florida in 2015. This indicates that both butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety.

### **Finding of Necessity of Schedule I Placement to Avoid Imminent Hazard to Public Safety**

In accordance with 21 U.S.C. 811(h)(3), based on the available data and information, summarized above, the continued uncontrolled manufacture, distribution, reverse distribution, importation, exportation, conduct of research and chemical analysis, possession, and abuse of butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for these substances in the United States. A substance meeting the statutory

requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed in schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for butyryl fentanyl and beta-hydroxythiofentanyl indicate that these substances have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated December 21, 2015, notified the Assistant Secretary of the DEA's intention to temporarily place this substance in schedule I.

## **Conclusion**

This notice of intent initiates an expedited temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA, 21 U.S.C. 811(h). In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein set forth the grounds for his determination that it is necessary to temporarily schedule butyryl fentanyl and beta-hydroxythiofentanyl in schedule I of the CSA, and finds that placement of these opioid substances into schedule I of the CSA is necessary in order to avoid an imminent hazard to the public safety.

Because the Administrator hereby finds that it is necessary to temporarily place these synthetic opioids into schedule I to avoid an imminent hazard to the public safety, any subsequent final order temporarily scheduling these substances will be effective on the date of publication in the *Federal Register*, and will be in effect for a period of two years,

with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h) (1) and (2). It is the intention of the Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this notice. Butyryl fentanyl and beta-hydroxythiofentanyl will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, research, conduct of instructional activities and chemical analysis, and possession of a schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done “on the record after opportunity for a hearing” conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

### **Regulatory Matters**

Section 201(h) of the CSA, 21 U.S.C. 811(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the *Federal*

*Register* of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary of HHS. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 553 of the APA, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of section 553 of the APA, the DEA notes that in accordance with 21 U.S.C. 811(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a “rule” as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act (RFA). The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by section 553 of the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

#### **List of Subjects in 21 CFR Part 1308**

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA proposes to amend 21 CFR Part 1308 as follows:

#### **PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES**

1. The authority citation for part 1308 continues to read as follows:

**Authority:** 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. In § 1308.11, add paragraphs (h) (26) and (27) to read as follows:

##### **§ 1308.11 Schedule I**

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(h) \* \* \*

(26) *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutyramide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: butyryl fentanyl).....(9822)

(27) *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide,  
its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: beta-  
hydroxythiofentanyl) .....(9836)

Dated: March 16, 2016

Chuck Rosenberg,

*Acting Administrator.*

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